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REMARKS

After entry of the present amendment, claims 1-9, 15-26, 32-36 and 41-42 are pending in the application. Claims 1, 4, 15, 19-22, 24-26, 35-36 and 41 are herein amended. Claims 12 and 14 are canceled herein. Claims 10, 11, 13, 27-31 and 37-40 were canceled in a previous amendment.

Claim 12 has been canceled to address antecedent basis issues that arose due to the amendment to claim 1. Claims 19-22 have been amended to depend on either claim 1 or claim 15, instead of claim 14, which is canceled herein.

At the outset, Applicants wish to thank the Examiner for speaking with the Applicants' representative, Attorney Todd Garabedian, on October 12, 2006. Per that discussion, Applicants have incorporated the Examiner's suggested amendments into claims 1, 4, 19-22, 24-26, 35-36 and 41.

Rejections under 35 USC §112

Claims 1-9, 12, 14-26, 32-36, 41 and 42 were rejected under 35 USC §112, second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter which applicant regards as the invention.

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Specifically, the Examiner indicated that it is not clear what Applicants intend as the "engineered protein" because the second wherein clause would appear redundant or superfluous unless Applicants intended the engineered antibody as encompassed.

Claims 1 and 35 are amended to more specifically define the term "engineered protein" and to remove the second wherein clause. Accordingly, Applicants submit the rejection is now moot and respectfully request the Examiner withdraw the rejection.

Rejections under 35 USC §102

Claims 1-9, 12, 32-36, 41 and 42 were rejected under 35 USC §102(b) as being anticipated by U.S. Patent No. 4,595,655 to Self.

Self discloses a method for determining a ligand or receptor. The ligand may be a partner of cell- and non-cell associated, non-antibody receptors. The term "non-antibody" receptor includes non-antibody receptors that are synthetically produced. (See col. 2, line 4 to col. 3, line 15).

Claims 1 and 35, and the claims dependent therefrom, have been amended to recite "wherein at least one of the first and second affinity ligands is an engineered protein, constructed

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from a scaffold domain selected from domains of bacterial receptins, fibronectins, protease inhibitors, retinol binding proteins, bilin binding proteins, amylase inhibitors, CTLA-4, cytochromes, or cellulose binding proteins." Support for these amendments can be found at least in originally presented claim 14. Accordingly, no new matter is added by this amendment.

Self does not teach or suggest a sandwich assay method using an engineered, combinatorial, scaffold-based protein as one or more affinity ligands. Accordingly, Applicants submit that Self, either taken alone or in combination with any other reference, does not disclose or suggest the sandwich assay method of the present claimed invention. Therefore, Applicants submit the present rejection has been overcome and respectfully request the Examiner withdraw the rejection.

Claims 1-8, 12, 32-36, 41 and 42 were rejected under 35 USC §102(b) as anticipated by U.S. Patent No. 5,284,778 to Canfield, et al.

Canfield, et al. discloses a quantitative assay for determining the amount of a biologically active ligand present in a sample. The assay includes contacting the sample with both the receptor to which the ligand naturally binds and a monoclonal antibody. (See col. 5, lines 24-40). The receptor may be synthesized. (See col. 6, lines 23-26).

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Claims 1 and 35, and the claims dependent therefrom, have been amended to recite "wherein at least one of the first and second affinity ligands is an engineered protein, constructed from a scaffold domain selected from domains of bacterial receptins, fibronectins, protease inhibitors, retinol binding proteins, bilin binding proteins, amylase inhibitors, CTLA-4, cytochromes, or cellulose binding proteins." Support for these amendments can be found at least in originally presented claim 14. Accordingly, no new matter is added by this amendment.

Canfield, et al. does not teach or suggest a sandwich assay method using an engineered, combinatorial, scaffold-based protein as one or more affinity ligands. Accordingly, Applicants submit that Canfield, et al., either taken alone or in combination with any other reference, does not disclose or suggest the sandwich assay method of the present claimed invention. Therefore, Applicants submit the present rejection has been overcome and respectfully request the Examiner withdraw the rejection.

Claims 1-4, 6-8, 12, 14-26, 32, 35, 36 and 41 were rejected under 35 USC §102(b) as being anticipated by Hansson, et al. (Immunotechnol. 4: 237, 1999).

In Hansson, et al. the most relevant experiments are epitope mapping studies in a Biacore™ instrument, in which a

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target-binding Z molecule is immobilized on a sensor chip surface, a target molecule is applied, and an antibody known to interact with the target is applied thereafter. The experiments are carried out using laboratory buffers, i.e., purified protein preparations. These experiments are described on pages 242 and 245-246.

In contrast, the presently claimed invention is a sandwich assay for detecting the presence of a target molecule in a sample that includes a complex biological fluid. The claimed sandwich assay requires indirect detection of a target molecule through the detection of the presence of the second affinity ligand. As discussed on page 2 of the present specification, the use of present capture immunoassays for detection and quantification of molecules in complex biological fluids presents problems such as false positive signals. An object of the present invention is to overcome the problems experienced when using immunoassays with complex biological fluids, e.g., reduction or elimination of false positives.

Applicants submit Hansson, et al. does not teach or suggest the detection of a target molecule in a sample comprising a complex biological fluid. Rather, the experiments in Hansson, et al. teach away from the presently claimed invention as they

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are carried out using a laboratory buffer, i.e., purified protein preparations.

Furthermore, Hansson, et al. does not teach or suggest the step of detecting the presence of the second affinity ligand, where such presence is an indicator of the presence of a target molecule in the sample. In fact, Applicants submit that detection of a second affinity ligand in the experiments of Hansson, et al. to detect the presence of a target molecule is not needed and such step would be redundant since the target molecule is detected instantaneously with the use of the surface plasmon resonance-based Biacore™ instrument.

Accordingly, Applicants submit the present rejection has been overcome and respectfully request the Examiner withdraw the rejection.

Claims 1-4, 6, 8, 12, 14-26, 32, 35, 36 and 41 were rejected under 35 USC §102(b) as being anticipated by International Patent Application No. WO 00/63243 to Ljungqvist, et al. Applicants respectfully traverse this rejection.

Ljungqvist, et al. discloses modified polypeptides which are derivatives of the B domain or Z domain from staphylococcal protein A (SPA). Between 1 and 20 amino acid residues of the B or Z domain have been substituted by other amino acid residues. The substitution was made without substantial loss of the basic

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structure and stability of the B or Z domain, and the substitution results in interaction capacity of the polypeptide with at least one domain of human Factor VIII protein.

In Ljungqvist, et al., the most relevant experiments are epitope mapping studies using a Biacore™ instrument, in which a target-binding Z molecule is immobilized on a sensor chip surface, a target molecule is applied, and an antibody known to interact with the target is applied thereafter. The experiments are carried out using laboratory buffers, i.e., purified protein preparations. These experiments are described on pages 11-13 and 16-17.

In contrast, the presently claimed invention is a sandwich assay for detecting the presence of a target molecule in a sample that includes a complex biological fluid. The claimed sandwich assay requires indirect detection of a target molecule through the detection of the presence of the second affinity ligand. As discussed on page 2 of the present specification, the use of present capture immunoassays for detection and quantification of molecules in complex biological fluids presents problems such as false positive signals. An object of the present invention is to overcome the problems experienced when using immunoassays with complex biological fluids, e.g., reduction or elimination of false positives.

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Applicants submit Ljungqvist, et al. does not disclose or suggest the detection of a target molecule in a sample comprising a complex biological fluid. Rather, the experiments in Ljungqvist, et al. teach away from the presently claimed invention as the experiments are carried out using laboratory buffers, i.e., purified protein preparations.

Furthermore, Ljungqvist, et al. does not teach or suggest the step of detecting the presence of the second affinity ligand, where such presence is an indicator of the presence of a target molecule in the sample.. In fact, Applicants submit that detection of a second affinity ligand in the experiments of Ljungqvist, et al. to detect the presence of a target molecule is not needed and such step would be redundant since the target molecule is detected instantaneously with the use of the surface plasmon resonance-based Biacore™ instrument.

Accordingly, Applicants submit the present rejection has been overcome and respectfully request the Examiner withdraw the rejection.

Applicants submit that the claims are now in condition for allowance and a prompt Notice of Allowance is respectfully solicited.

If the Examiner believes a telephone conference would aid in the continued prosecution of this application, the Examiner

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is invited and encouraged to contact Applicants' representative at the telephone number listed below.

Any fees due with this correspondence may be charged to Deposit Account 23-1665 under Customer Number 27267.

Respectfully submitted,

Niklas Ahlberg, et al.

Date: October 16, 2006

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